

Draxin: a novel player in the molecular control of cranial neural crest EMT

Erica J. Hutchins and Marianne E. Bronner, Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA 91125*

ABSTRACT: Neural crest (NC) cells, which generate the sensory and autonomic ganglia of the peripheral nervous system and the craniofacial skeleton among other derivatives, undergo a spatiotemporally regulated epithelial-to-mesenchymal transition (EMT) to delaminate from the neural tube, with a sequence of initiation that progresses from rostral to caudal. Here, we show the secreted molecule Draxin, an established repulsive axon guidance molecule, acts to modulate Wnt signaling downstream of NC specification to control the timing of cranial NC EMT. Endogenous draxin is expressed in a coordinated wave along the axis, where its expression initiates after neural crest specification and is downregulated just prior to cranial NC delamination. Functional experiments show that Draxin controls the timing of cranial NC EMT via canonical Wnt signaling modulation. Ectopic maintenance of Draxin expression resulted in reduced NC emigration from the neural tube, implicating a repressive role for Draxin in controlling NC EMT. Reciprocally, loss of Draxin triggered premature NC EMT. Modulating Draxin expression also altered canonical Wnt reporter activity in vivo. Accordingly, coexpression of Draxin plus either activated β -catenin or LRP5, both components of the canonical Wnt pathway, was able to rescue NC EMT and emigration. Taken together, these data indicate Draxin acts as a molecular rheostat of canonical Wnt signaling required to regulate the precise timing of initiation and completion of cranial neural crest EMT.

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Erica Hutchins
Postdoctoral scholar
Bronner Group